

**IN THE CLAIMS**

Please amend the claims as follows:

1. Currently Amended) A system, comprising:

an implantable gene regulatory signal delivery device that emits, in response to a gene regulatory control signal, a regulatory signal which regulates transcription from a regulatable transcriptional control element;

an implantable cardiac rhythm management (CRM) device including:

a sensor to sense a physiological signal indicative of a predetermined cardiac condition;

an event detector configured to detect the predetermined cardiac condition from the sensed physiological signal and produce one or more condition parameters related to one of a type and a degree of the predetermined cardiac condition;

and

a controller coupled to the sensor and electrically connected to the gene regulatory signal delivery device, the controller configured to produce the gene regulatory control signal, transmit the gene regulatory signal to the gene regulatory signal delivery device to trigger an emission of the regulatory signal in response to a detection of the predetermined cardiac condition, and quantitatively control the emission of the regulatory signal based on the one or more condition parameters, ~~wherein the controller is electrically wired to the gene regulatory signal delivery device; and~~

one or more implantable leads providing for electrical connections between the implantable gene regulatory signal delivery device and the implantable CRM device,

wherein the controller is electrically wired to the gene regulatory signal delivery device through the electrical connections, and

wherein the regulatory signal is selected to regulate the regulatable transcriptional control element in a vector having the regulatable transcriptional control element operably linked to an open reading frame, the expression of which treats the predetermined cardiac condition.

2. (Previously Presented) The system of claim 1, wherein the gene regulatory signal delivery device comprises an electric field generator which emits an electric field as the gene regulatory signal.

3. (Previously Presented) The system of claim 1, wherein the gene regulatory signal delivery device comprises an electromagnetic field generator which emits an electromagnetic field as the gene regulatory signal.

4. (Previously Presented) The system of claim 1, wherein the gene regulatory signal delivery device comprises a light emitter which emits a light having a predetermined wavelength and energy.

5. (Previously Presented) The system of claim 1, wherein the gene regulatory signal delivery device comprises a speaker which emits an acoustic energy.

6. (Previously Presented) The system of claim 1, wherein the gene regulatory signal delivery device comprises a drug delivery device which contains a chemical agent.

7. (Previously Presented) The system of claim 1, wherein the gene regulatory signal delivery device comprises a thermal radiator which emits a thermal energy.

8-9. (Canceled)

10. (Previously Presented) The system of claim 1, wherein the sensor comprises an electrogram sensing circuit, and the event detector comprises an arrhythmia detector.

11. (Original) The system of claim 10, wherein the event detector comprises an atrial fibrillation detector.

12. (Original) The system of claim 10, wherein the event detector comprises a ventricular fibrillation detector.

13. (Previously Presented) The system of claim 1, wherein the sensor comprises a sensor sensing a physiological signal indicative of ischemia, and the event detector comprises an ischemia detector.

14. (Previously Presented) The system of claim 1, wherein the sensor comprises a metabolic sensor adapted to sense a signal indicative of a cardiac metabolic level.

15. (Previously Presented) The system of claim 14, wherein the sensor comprises at least one of a pH sensor, an oxygen pressure (PO<sub>2</sub>) sensor, a carbon dioxide pressure (PCO<sub>2</sub>) sensor, a glucose sensor, a creatine sensor, a C-creative protein sensor, a creatine kinase sensor, and a creatine kinase-MB sensor.

16. (Previously Presented) The system of claim 1, wherein the sensor comprises an impedance sensor to sense tissue impedance.

17. (Previously Presented) The system of claim 16, wherein the impedance sensor comprises a pulmonary impedance sensor.

18. (Previously Presented) The system of claim 17, wherein the impedance sensor comprises a respiratory sensor.

19. (Previously Presented) The system of claim 1, wherein the sensor comprises a pressure sensor to sense a pressure in a cardiovascular system.

20. (Previously Presented) The system of claim 19, wherein the pressure sensor comprises at least one of a left atrial pressure sensor, a left ventricular pressure sensor, an artery pressure sensor, and a pulmonary arterial pressure sensor.

21. (Previously Presented) The system of claim 20, wherein the event detector comprises a systolic dysfunction detector.

22. (Previously Presented) The system of claim 20, wherein the event detector comprises a diastolic dysfunction detector.

23. (Previously Presented) The system of claim 1, wherein the sensor comprises a stroke volume sensor.

24. (Previously Presented) The system of claim 1, wherein the sensor comprises a neural activity sensor.

25. (Previously Presented) The system of claim 24, wherein the neural activity sensor comprises a neurohormone sensor to sense a neurohormone level.

26. (Previously Presented) The system of claim 24, wherein the neural activity sensor comprises an action potential recorder to sense neural electrical activities.

27. (Previously Presented) The system of claim 1, wherein the sensor comprises a heart rate variability detector.

28. (Previously Presented) The system of claim 1, wherein the sensor comprises a renal function sensor.

29. (Previously Presented) The system of claim 28, wherein the renal function sensor comprises at least one of a renal output sensor, a filtration rate sensor, and an angiotensin II level sensor.

30. (Previously Presented) The system of claim 1, wherein the sensor comprises an acoustic sensor adapted to sense at least one of heart sounds and respiratory sounds.

31. (Previously Presented) The system of claim 30, wherein the event detector to detect the predetermined cardiac condition when third hear sound (S3) amplitude exceeds a predetermined threshold.

32. (Currently Amended) A system, comprising:

an implantable gene regulatory signal delivery device that emits, in response to a gene regulatory control signal, a regulatory signal which regulates transcription from a regulatable transcriptional control element; and

an implantable medical device system including:

a sensor to sense a physiological signal indicative of a predetermined cardiac condition;

an event detector configured to detect the predetermined cardiac condition from the sensed physiological signal and produce one or more condition parameters related to at least one of a type and a degree of the predetermined cardiac condition;

an implant telemetry module to receive an external command;

and

an implant controller coupled to the sensor and the implant telemetry module, the implant controller configured to quantitatively control the emission of the regulatory signal based on the one or more condition parameters and the external command, ~~wherein the implant controller is electrically wired to the gene regulatory signal delivery device; one or more implantable leads providing for electrical connections between the implantable gene regulatory signal delivery device and the implantable medical device,~~

~~one or more implantable leads providing for electrical connections between the implantable gene regulatory signal delivery device and the implantable medical device wherein the implant controller is electrically wired to the gene regulatory signal delivery device through the electrical connections; and~~

an external system including:

an external telemetry module to transmit the external command to the implant telemetry module;

a user input device adapted to receive the external command; and

an external controller adapted to automatically analyze signals acquired by the implantable medical device and generate the external command when deemed necessary as a result of the analysis,

wherein the regulatory signal is selected to regulate a regulatable transcriptional control element in a vector having the regulatable transcriptional control element operably linked to an open reading frame, the expression of which in an effective amount treats the predetermined cardiac condition.

33. (Previously Presented) The system of claim 32, wherein the gene regulatory signal delivery device comprises an electric field generator which emits an electric field being the regulatory signal.

34. (Previously Presented) The system of claim 32, wherein the gene regulatory signal delivery device comprises an electromagnetic generator which emits an electromagnetic field as the gene regulatory signal.

35. (Previously Presented) The system of claim 32, wherein the gene regulatory signal delivery device comprises a light emitter which emits a light having a predetermined wavelength and energy.

36. (Previously Presented) The system of claim 32, wherein the gene regulatory signal delivery device comprises a speaker which emits an acoustic energy.

37. (Previously Presented) The system of claim 32, wherein the gene regulatory signal delivery device comprises a drug delivery device which contains a chemical agent.

38. (Previously Presented) The system of claim 32, wherein the gene regulatory signal delivery device comprises a thermal radiator which emits a thermal energy.

39-40. (Canceled)

41. (Previously Presented) The system of claim 32, wherein the sensor comprises an electrogram sensing circuit, and the event detector comprises an arrhythmia detector.

42. (Previously Presented) The system of claim 41, wherein the event detector comprises an atrial fibrillation detector.

43. (Previously Presented) The system of claim 41, wherein the event detector comprises a ventricular fibrillation detector.

44. (Previously Presented) The system of claim 32, wherein the sensor comprises a sensor sensing an physiological signal indicative of ischemia, and the event detector comprises an ischemia detector.

45. (Previously Presented) The system of claim 32, wherein the sensor comprises a metabolic sensor adapted to sense a signal indicative of a cardiac metabolic level.

46. (Previously Presented) The system of claim 45, wherein the sensor comprises at least one of a pH sensor, an oxygen pressure (PO<sub>2</sub>) sensor, a carbon dioxide pressure (PCO<sub>2</sub>) sensor, a glucose sensor, a creatine sensor, a C-creative protein sensor, a creatine kinase sensor, and a creatine kinase-MB sensor.

47. (Previously Presented) The system of claim 32, wherein the sensor comprises an impedance sensor to sense tissue impedance.

48. (Previously Presented) The system of claim 47, wherein the impedance sensor comprises a pulmonary impedance sensor.

49. (Previously Presented) The system of claim 48, wherein the impedance sensor comprises a respiratory sensor.

50. (Previously Presented) The system of claim 32, wherein the sensor comprises a pressure sensor to sense a pressure in a cardiovascular system.

51. (Previously Presented) The system of claim 50, wherein the pressure sensor comprises at least one of a left atrial pressure sensor, a left ventricular pressure sensor, an artery pressure sensor, and a pulmonary arterial pressure sensor.

52. (Previously Presented) The system of claim 51, wherein the event detector comprises a systolic dysfunction detector.

53. (Previously Presented) The system of claim 51, wherein the event detector comprises a diastolic dysfunction detector.

54. (Previously Presented) The system of claim 32, wherein the sensor comprises a stroke volume sensor.

55. (Previously Presented) The system of claim 39, wherein the sensor comprises a neural activity sensor.

56. (Previously Presented) The system of claim 55, wherein the neural activity sensor comprises a neurohormone sensor to sense a neurohormone level.

57. (Previously Presented) The system of claim 55, wherein the neural activity sensor comprises an action potential recorder to sense neural electrical activities.

58. (Previously Presented) The system of claim 32, wherein the sensor comprises a heart rate variability detector.

59. (Previously Presented) The system of claim 32, wherein the sensor comprises a renal function sensor.

60. (Previously Presented) The system of claim 59, wherein the renal function sensor comprises at least one of a renal output sensor, a filtration rate sensor, and an angiotensin II level sensor.

61. (Previously Presented) The system of claim 32, wherein the sensor comprises an acoustic sensor adapted to sense at least one of heart sounds and respiratory sounds.

62. (Previously Presented) The system of claim 61, wherein the event detector to detect the predetermined cardiac condition when third hear sound (S3) amplitude or activity exceeds a predetermined threshold level.

63. (Previously Presented) The system of claim 32, wherein the implantable medical device system further comprises a pacing circuit coupled to the implant controller, and wherein the implant controller includes a pacing control module adapted to control a delivery of pacing pulses in conjunction with the emission of the regulatory signal.

64. (Previously Presented) The system of claim 63, wherein the pacing control module is further adapted to control the delivery of pacing pulses based on at least the external command.

65. (Previously Presented) The system of claim 63, wherein the implantable medical device system further comprises a cardiac resynchronization therapy (CRT) circuit coupled to the implant controller, and wherein the implant controller includes a CRT control module adapted to control a delivery of CRT in conjunction with the emission of the regulatory signal.

66. (Previously Presented) The system of claim 63, wherein the implantable medical device system further comprises a remodeling control (RCT) therapy circuit coupled to the implant controller, and wherein the implant controller includes a RCT therapy control module adapted to control a delivery of RCT therapy in conjunction with the emission of the regulatory signal.

67. (Previously Presented) The system of claim 63, wherein the implantable medical device system further comprises a defibrillation circuit coupled to the implant controller, and wherein the implant controller includes a defibrillation control module adapted to control a delivery of cardioversion/defibrillation shocks in conjunction with the emission of the regulatory signal.

68. (Previously Presented) The system of claim 67, wherein the defibrillation control module is further adapted to control the delivery of cardioversion/defibrillation shocks based on at least the external command.

69. (Previously Presented) The system of claim 67, further comprising at least one atrial defibrillation lead coupled to the defibrillation circuit to deliver the defibrillation shocks to one or more atria, and wherein the defibrillation control module comprises an atrial defibrillation control module.

70. (Previously Presented) The system of claim 67, further comprising at least one ventricular defibrillation lead coupled to the defibrillation circuit to deliver the defibrillation shocks to one or more ventricles, and wherein the defibrillation control module comprises a ventricular defibrillation control module.

71. (Previously Presented) The system of claim 32, wherein the implantable medical device system comprises a hermetically sealed can to house at least the implant controller and the implant telemetry module.

72. (Previously Presented) The system of claim 71, wherein the hermetically sealed can further houses the sensor.

73. (Previously Presented) The system of claim 71, wherein the sensor is external to the hermetically sealed can.

74. (Previously Presented) The system of claim 32, wherein the external system comprises:

- a presentation device to present the sensed physiological signal; and
- a user input device to receive the external command.

75. (Previously Presented) The system of claim 74, wherein the external system comprises a programmer.

76. (Previously Presented) The system of claim 74, wherein the external system comprises an advanced patient management system including:

- an external device wirelessly coupled to the implantable medical device system via telemetry;
- a remote device to provide for access to the implantable medical device system from a distant location; and
- a network connecting the external device and the remote device.

77. (Previously Presented) The system of claim 76, wherein the external device comprises the user input.

78. (Previously Presented) The system of claim 76, wherein the remote device comprises the user input.

79-149. (Canceled)

150. (Previously Presented) The system of claim 1 or 32 wherein the vector is not part of an implantable device.

151. (Previously Presented) The system of claim 1 or 32 wherein the controller comprises a timer adapted to time a predetermined period of delivery time during which the gene regulatory signal delivery device emits the regulatory signal.

152. (Previously Presented) The system of claim 1, wherein the controller is adapted to quantitatively control the emission of the regulatory signal using parameters defining type and energy of the regulatory signal.